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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,849	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-122 is/are pending in the application.

4a) Of the above claim(s) 1,2,13,14,23,24,33,34,45,46,57 and 58 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 3-12,15-22,25-32,35-44,47-56 and 59-68 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-122 are pending. Claims 1, 2, 13, 14, 23, 24, 33, 34, 45, 46, 57 and 58, drawn to non-elected inventions, remain withdrawn from consideration. Claims 2-4, 9, 10, 21, 31, 33-36, 41, 45-48, 53, 57-60 and 65 have been amended. Claims 3-12, 15-22, 25-32, 35-44, 47-56 and 59-68 are under consideration. Claims 4, 5, 10, 12, 22, 32, 36, 37, 42, 43, 48, 49, 54, 55, 60, 61, 65 and 66 are under consideration to the extent that they read on SEQ ID NO:3.

2. Claims 4, 5, 10, 12, 22, 32, 36, 37, 42, , 43, 48, 49, 54, 55, 60, 61, 66 and 67 are objected to for reciting non-elected inventions. Appropriate correction is required. It is noted that the restriction requirement for a single sequence was not an election of species.

3. Claims 3-12, 15-22, 25-32, 35-44, 47-56 and 59-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1-4 have been amended to delete the phrase "of classifying a tumor" from the method objective. Claims 33-36, 45-48, 57-60 have been amended to delete the phrase "of testing a subject" from the method objective. The deletion of the method objective results in a claim that is broader in scope than the originally filed claims because the method steps can be construed to be part of any method irregardless of the method objective and this scope is not supported by the specification as filed which does not teach the instant methods as part of other broader methods.

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 3-12, 15-22, 25-32, 35-44, 47-56 and 59-68 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-4 and 10 recite a method, the culmination of which results in the classification of a tumor "based on" the results of the detecting step. Claim 10 is further drawn to a method, the culmination of which results in stratifying the subject for a clinical trial based on the results of the classifying step. Claims 16 and 17 further recite providing diagnostic, prognostic or predictive information based on the classifying step. Claims 33-36 are drawn to a method, the culmination of which results in providing diagnostic, prognostic or predictive information based on the results of the detecting step. Claims 45-48 are drawn to methods, the culmination of which results in stratifying the subject for a clinical trail based on the results of the detecting step. Claims 58-60 are drawn to a method, the culmination of which results in the selection of a treatment based on the results of the detecting step. Thus the claims culminate in a step which requires abstract reasoning on the part of the routineer because an active method step based on a tangible measurement is not encompassed in the final step. The MPEP (2106) states:

"For such subject matter to be statutory, the claimed process must be limited to a practical application of the abstract idea or mathematical algorithm in the technological arts. See Alappat, 33 F.3d at 1543, 31USPQ2d at 1556-57 (quoting Diamond v. Diehr, 450 U.S. at 192, 209 USPQ at 10). See also Alappat 33 F.3d at 1569, 31 USPQ2d at 1578-79 (Newman, J., concurring) ("unpatentability of the principle does not defeat patentability of its practical applications") (citing In Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980) the court held that abstract ideas are not patentable. A scientific principle, divorced from any tangible structure, can be rejected as not within the statutory classes. O 'Reilly v. Morse, 56 U.S. (15 How.) 62 (1854). A process that consists solely of the manipulation of an abstract idea is not concrete or tangible. See In re Warmerdam, 33 F.3d 1354, 1360, 31 USPQ2d 1754, 1759 (Fed. Cir. 1994). See also Schrader, 22 F.3d at 295, 30 USPQ2d at 1459"

and

"Only when the claim is devoid of any limitation to a practical application in the technological arts should it be rejected under 35 U.S.C. 101. Compare Musgrave, 431 F.2d at 893, 167 USPQ at 289; In re Foster, 438 F.2d 1011, 1013, 169 USPQ 99, 101 (CCPA 1971)"

Thus, classifying, stratifying, providing information and selecting a treatment are all thought processes which are not connected by means of a tangible correlation to the results of the previous step. Applicant is advised to amend the claims in such as way as to specifically relate the positive detection or quantitation of the protein with the positive or negative presence of a specific cancer, or a positive or negative prognostic indication of the patient.

6. Claims 3, 4-10, 15-22, 25-31, 35-43, 47-55, 59-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of classifying a breast

tumor, and a method of testing for breast cancer comprising the detection of SEQ ID NO:3 or the polynucleotide encoding SEQ ID NO:3, does not reasonably provide enablement for a method of classifying any tumor or a method of detecting any type of cancer comprising detecting SEQ ID NO:3 or the polynucleotide encoding SEQ ID NO:3.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims are drawn to methods of classifying a tumor in a subject, methods of testing a subject, all methods comprising the detection of SEQ ID NO:3 or a gene encoding SEQ ID NO:3. the specification teaches that SEQ ID NO:3 is associated with a basal tumor subtype in breast tumors. The specification does not provide a description of tumors from any other organ which would express SEQ ID NO:3 as a diagnostic, prognostic marker. The genus of tumors encompassed by the claims is highly variant because it includes all tumor types. Further, the genus of methods of testing a subject is even more variant, said method not confined to the testing of tumors, but encompasses the testing of bodily fluids such as blood, serum, urine and ascites. The art acknowledges that tumors are heterogeneous and much variation between tumor samples is possible within a tumor of the same type and within a given tissue and/or organ. Thus, one of skill in the art would reasonably conclude that the variation between tumors within in different tissues and organs is immense Thus, there is no nexus between the expression of SEQ ID NO:3 in a breast tumor and the expression of SEQ ID NO: in a non-breast tumor such as a carcinoma in another tissue type, a sarcoma, melanoma or a lymphoma. This is a pattern which is common in the art as exemplified by the abstract of Vlasoff et al (Appl Immunohistochem Mol Morphol. 2002 Sep;10(3):237-41) which teaches that in hepatocellular tumors, c-erbB2 is neither over expressed or up regulated and is not a prognostic factor, in contrast with the abstract of Ross and Fletcher (Stem Cells. 1998;16(6):413-28) which teaches the diagnostic and prognostic relevance of ever expression of c-erbB2 (Her-2) in breast cancer. It logically follows that in order to provide prognostic, diagnostic or otherwise predictive information to the subject, it would be necessary to first know if SEQ ID NO:3 were expressed in other tumors beyond the subtype of breast tumors disclosed by the instant specification. Further, the art acknowledges that the use of prognostic markers is specifically tied to the type of cancer expressing said marker. For instant the abstract of Herms et al (Int J Cancer. 2000 Sep 20;89(5):395-402)

teaches that expression of c-myc in a brain tumor is an independent predictive factor of death from medulloblastoma. This is in contrast to the abstract of Matsumoto et al (Int J Colorectal Dis. 1993 Jul;8(2):103-5) which teaches that c-myc is not a prognostic factor for colorectal carcinomas. Thus, the prognosis associated with the expression of SEQ ID NO:3 in a breast tumor would not anticipate the prognosis associated with SEQ ID NO:3 in a non-breast tumor, and the up regulation of SEQ IDNO:3 in breast tumor tissue in no way anticipates the up regulation of SEQ ID NO:3 in non-tumor tissue. Therefore, one of skill in the art would be forced into undue experimentation in order to practice the broadly claimed methods as they pertain to tumors which are not breast tumors.

7. The rejection of claims 3-6, 9, 12, 15-18, 21, 22, 35-38, 41-44, 67 and 68 under 35 U.S.C. 102(b) as being anticipated by Hackett et al (US 5,158,893) is withdrawn in light of applicants arguments.

8. The rejection of claims 35-39, 42 and 43 under 35 U.S.C. 102(b) as being anticipated by Soppet (WO 98/21242) is maintained for reasons of record.

Claims 35 and 36 are drawn to a method of testing a subject comprising the steps of providing a sample isolated from a subject having a tumor; detecting the expression or activity of a gene encoding the polypeptide of SEQ ID NO:3 in the sample and providing diagnostic, prognostic or predictive information about the subject based on the results of the detecting step. Claim 37 embodies the methods of claims 35 and 36 wherein the detecting step comprises detecting the polypeptide. Claims 38 embodies the method of claim 37 wherein the polypeptide is detected by an immunohistochemical analysis using an antibody that specifically binds to the polypeptide. Claim 39 embodies the method of claim 37 wherein the polypeptide is detected by using an ELISA assay and an antibody which specifically binds to the polypeptide. Claim 42 embodies the methods of claims 35 or 36 wherein the sample is blood, urine, serum, ascites, saliva, a cell or a portion of tissue. Claim 43 embodies the method of claim 35 or 36 wherein the sample is a tumor sample.

Soppet discloses a method for detecting cancer comprising detecting the over expression of the calcitonin receptor (page 29, lines 9-16). Soppet discloses that the assaying of the

calcitonin receptor levels in a tissues can be studies by immunohistochemical methods (page 29, lines 23-27) and by ELISA assay (page 30, lines 1-3). Soppet specifically discloses epitope-bearing portions of the calcitonin receptor as including ammo acid residues 49-60, 113-123, 145-154, 189-209 and 259 to 560 of sequence identifier 2. The residues 2388-2921 of the instant SEQ ID NO:3 are identical to residues 33-566 of the sequence identifier 2. Thus, antibodies which bind to said specific epitopes of the calcitonin receptor will also bind to the instant SEQ ID NO:3.

Applicant argues that Soppet cannot anticipate the claimed method because Soppet et al does not provide an enabling disclosure. Applicant states that Soppet et al does not provide providing diagnostic, prognostic or predictive information about the subject based on the detecting step. This has been considered but not found persuasive. The rejected claims require only that diagnostic information about the subject be provided as the terms diagnostic, prognostic or predicting information about the subject is clearly referred to in the alternative. Thus, the detection of the protein encoded by the polynucleotide disclosed by Soppet et al need only be correlated with the likelihood of a tumor in order to provide diagnostic information about the subject.

Applicant argues that the disclosure of Soppet is not enabling because the disclosure identifies a multitude of diseases of conditions which are indicated by an over expression of the calcitonin receptor on page 29, lines 9-16. The examiner notes that "cancer" is one of the diseases. Applicant argues that the protein encoded by the polynucleotide disclosed by Soppet et al is hypothetical. This has been considered but not found persuasive. Applicant has not provided any data or arguments to refute the fact that over expression of the polynucleotide encoding the protein of Soppet et al would not result in over expression of the hypothetical protein.

9. It is also noted that the instant claims are widely drawn to encompass any form of cancer, rather than being limited to breast tumors. Amendment of the claims to breast cancer, rather than generic cancer would overcome the above rejection.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
10/4/2004

KAREN A. CANELLA PH.D
PRIMARY EXAMINER